REMARKS

Applicants respectfully request reconsideration based on the amendments above and the remarks that follow.

Status of the Claims:

Claims 1-102 were pending in the application, with claims 1-88 being withdrawn from consideration. Claims 89, 91, 93, and 97-99 have been amended to overcome the section 112-first and second paragraph rejections. No claims have been canceled or newly added.

A detailed listing of the claims along with their appropriate status identifiers are presented for the Examiner's consideration.

I. Double Patenting:

Claims 89, 91 and 93 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 42, 43, 45 and 47-49 of copending Application No. 10/555310 in view of US Patent NO. 5,840,332.

The present application claims priority to PCT/IL2003/00862 filed October 23, 2003. In contrast the '310 application filed December 22, 2006, claims priority to PCT/IL2003/01056, filed December 11, 2003. Applicants note that provisional rejections based on this ground are provided for in the MPEP, but should be removed when the rejection is the only rejection remaining in the application. See MPEP § 804. Applicants request removal of this rejection following reconsideration and withdrawal of the other rejections.

II. Rejections Under 35 U.S.C. § 112-First Paragraph:

Claims 89-102 are rejected for failing to comply with the written description requirement. Applicants respectfully traverse.

At the very outset, Applicants would like to thank the Examiner for indicating that Figure 14A-B and 15A-B support functional language in the inventive method, as it applies

to the phrases "substantially no release of venlafaxine....for two hours" and the release of "at least...60% of venlafaxine.... after the delayed burst". See Office Action at page 5. At issue, therefore is the Examiner's confusion about the formulation(s) that provide the release profiles graphically depicted in Figures 14A-B and 15A-B. Examiner Westerberg is further heard to seek clarification if "the data in example 1-6 are for separate dosage forms of the same formulation."

The claimed invention relates to a method for providing release of venlafaxine over a twenty-four hour period. To achieve this release profile, the inventive methodology recites to a delayed burst release formulation having a core and an outer coating. Specifically, the core includes venlafaxine, at least one burst control agent and an disintegrant. The outer coating comprises a water insoluble hydrophobic carrier and a water insoluble but hydrophilic particulate matter.

The delayed burst release formulation used in the inventive method, thus, encompasses a "genus", the individual species of which are represented by the choice of each component of the recited formulation.

The specification clearly describes the materials that can be used as burst control agents, disintegrants, and materials that can be used for the hydrophobic and hydrophilic components of the outer layer. For example, pages 7 - 9 of published PCT application No. WO 2004/037226, provides exemplars of compounds that are suitable as disintegrants, burst control agents and as components of the outer coating. By choosing an appropriate compound for each component of the recited formulation used in the inventive method, a person of ordinary skill, can readily practice and use the claimed invention without detracting from its teachings. Moreover, the skilled artisan would readily understand the specification and working examples to suggest that Applicants were in possession of the claimed invention. Applicants therefore respectfully request reconsideration and withdrawal of these rejections.

III. Rejections Under 35 U.S.C. § 112-Second Paragraph:

Claims 89-102 are rejected as being indefinite. Specifically, the Examiner has objected to the phrases "at least about two hours" and "substantially no" in claims 89, 91 and

93. Without acquiescing to the propriety of this rejection and in a good faith attempt to forward prosecution Applicants have deleted the phrase "at least about" from the identified claims.

Applicants however disagree with the alleged indefiniteness rejection of the phrase "substantially no." Contrary to the Examiner's assertion, this phrase, in the context of the claimed invention, would be readily understood by a person of ordinary skill to mean that "a considerable amount of venlafaxine would not be released.....for two hours." Stated differently, most of the venlafaxine will not be released and the amount that is in the two hour period is statistically insignificant and would not detract from the teachings of the claimed invention.

Besides, claim terms must be given their plain meaning as described in MPEP § 2111.01:

> *"During examination, the claims must be interpreted as broadly as their terms reasonably allow. In re American Academy of Science Tech Center, 367 F.3d 1359, 1369, 70 USPQ2d 1827, 1834 (Fed. Cir. 2004)."*
>
> *"This means that the words of the claim must be given their plain meaning.... In re Zletz, 893 F.2d 319, 321, 13 USPQ2d 1320, 1322 (Fed. Cir. 1989) (discussed below); Chef America, Inc. v. Lamb-Weston, Inc., 358 F.3d 1371, 1372, 69 USPQ2d 1857 (Fed. Cir. 2004)* ***(Ordinary, simple English words whose meaning is clear and unquestionable,*** *absent any indication that their use in a particular context changes their meaning,* ***are construed to mean exactly what they say.*** (Emphasis added).

Thus, the phrase "substantially no" is definite and would be understood by a person of ordinary skill. The rejection is improper and Applicants respectfully request its withdrawal.

Claims 97-99 are also rejected as being indefinite. Specifically, the Examiner has objected to the phrase "at least about 60%" in claims 97-99. Without acquiescing to the propriety of this rejection and in a good faith attempt to forward prosecution Applicants have deleted the phrase "about" from the identified claims. Applicants further state that the objected phrase would be

readily understood by a skilled artisan to indicate that "60% and up to 100% of venlafaxine is released in the recited time.

In view of the amendments to the claims, Applicants respectfully request withdrawal of this rejection.

IV. Rejections Under 35 U.S.C. § 103(a)

Claims 89-93 are rejected under 35 U.S.C. 103(a) as allegedly being unpatentable over U.S. Patent Number 6,274,171 to Sherman *et al.* (hereafter "Sherman") in view of U.S. Patent Number 5,840,332 to Lerner *et al.* (hereafter "Lerner"). Applicants respectfully traverse.

The formulation of venlafaxine used in the inventive methodology comprises from the inside out:

(a) a core formed as a compressed tablet comprising

(i) venlafaxine or a its pharmaceutically acceptable salt,

(ii) a disintegrant,

(ii) a burst control agent; and

(b) an outer coating comprising

(i) a water insoluble hydrophobic carrier, and

(ii) a water insoluble but hydrophilic particulate matter.

Such a formulation has certain advantages, such as diminished side effects, substantially no drug release for 2 hours and a burst release after 2 hours which release at least 60% of venlafaxine in the successive hour. Neither Sherman nor Lerner individually or in combination disclose the use of the recited formulation according to the claimed method. Importantly, the PTO has failed its duty of informing the Applicants why a skilled artisan would be motivated to combine Sherman and Lerner to arrive at the claimed invention, especially, in light of the absence of any suggestion in either reference for modifying the disclosed formulation.

The Office acknowledges that "the release profile of venlafaxine is determined by the physical structure and components of the pharmaceutical preparation." Office Action at page 9. The PTO further states that the combined teachings of the cited prior art teach a venlafaxine formulation as recited in the claims. Yet, Sherman or Lerner as acknowledged

by the PTO do not teach a "a substantially even blood plasma concentration of venlafaxine" a property displayed by the recited formulation.

Even if a skilled artisan were to accept the PTO's assertion that "the limitations regarding venlafaxine release .....must be inherently met as both the instant claims and the cited prior art recite a coated core venlafaxine formulation ....with the outer coating", the PTO fails to explain why the prior art formulation does not display the same advantageous physiological properties of the formulation recited in the claims.

> *"To establish inherency, the extrinsic evidence must make clear that the missing descriptive matter is necessarily present in the thing described in the reference, and that it would be so recognized by persons of ordinary skill. Inherency may not be established by probabilities or possibilities, however.* ***The mere fact that a certain thing may result from a given set of circumstances is not sufficient.*** *" In re Robertson, 169 F.3d 743, 745, 49 USPQ2d 1949, 1950-51 (Fed. Cir. 1999) (citations omitted).*

Sherman is directed to an extended release dosage formulation of venlafaxine hydrochloride. However, Sherman does not teach or suggest a substantially even blood plasma concentration of venlafaxine for an extended period of time. As illustrated in Table 3 of Sherman, the extended release tablets of Sherman result in a blood plasma concentration that substantially varies over the first four hours following administration. The changes in blood plasma levels of venlafaxine over subsequent four hour time periods are even larger.

Lerner, directed to a gastrointestinal delivery system comprising a core and a coating material, fails to resolve this deficiency of Sherman.

Applicants therefore submit that the outstanding rejection of claim 89 is improper, and respectfully request the Examiner to withdraw the same.

Claims 91 and 93 recite a method for releasing venlafaxine over a 24 hour period with diminished side effects, and a method for obtaining improved patient compliance respectively. Claims 91 and 93 also recite a formulation of claim 89, namely, one that comprises a core and an outer layer.

The same reasons mentioned above for obviating the obviousness rejection of claim 89, also apply here. Thus, claims 91 and 93 are also patentable over the combined teachings of Lerner and Sherman.

If an independent claim is non-obvious under § 103, then any claim depending therefrom is non-obvious. *In re Fine*, 5 USPQ2d 1596 (Fed. Cir. 1988). See MPEP 2143.03. Thus, Applicants submit that claims 90, 92, and 94-99 which depend from independent claims 89, 91 and 93 respectfully, are also non-obvious at least by virtue of their dependency from these claims.

Claims 89-102 are rejected under 35 U.S.C. 103(a) as allegedly being unpatentable over Sherman and Lerner as applied to claims 89-99 and further in view of U.S. Patent Number 5,506,270 to Upton *et al.* Applicants respectfully traverse.

Upton is cited as teaching that the recommended dose of venlafaxine is between 25 mg/day to 200 mg/day, which the Examiner opines reads on the 60 mg dose recited in claims 99-102. As stated above, neither Sherman nor Lerner or the combined teachings of these two references would allow a skilled artisan to arrive at the inventive method. Upton does not remedy the deficiencies of Sherman and Lerner combined. Moreover, as shown in Table 3 of the Sherman patent, there is a substantial variation in blood plasma level of venlafaxine using extended the release formulation, with blood plasma levels decreasing substantially over the 24 hour period. This data, surely would not prompt a physician or a formulations chemist to use a formulation that has a lower dose of venlafaxine as recited in the claims. The Examiner has used hind-sight to arrive at the claimed invention, and such use is impermissible by law. The pending claims are patentable in view of the combined teaching of Sherman, Lerner and Upton, and Applicants respectfully request reconsideration and withdrawal of the outstanding rejection under § 103.

CONCLUSION

Applicants believe that the present application is in condition for allowance and request an early indication of the same. Should any issues that warrant further reconsideration remain, then the examiner is requested to contact the undersigned attorney.

The Commissioner is hereby authorized to charge any additional fees which may be required regarding this application under 37 C.F.R. §§ 1.16-1.17, or credit any overpayment, to Deposit Account No. 19-0741. Should no proper payment be enclosed herewith, then the Commissioner is authorized to charge the unpaid amount to the same deposit account. If any extensions of time are needed for timely acceptance of papers submitted herewith, Applicants hereby petition for such extension under 37 C.F.R. §1.136 and authorizes payment of any such extensions fees to the deposit account.

Respectfully submitted,

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